CLAIM AMENDMENT

Please amend the claims as set forth below:

1. (Currently amended) A method for detecting at least a first isoprenylated protein in a cell comprising:

a) obtaining a synthetic isoprenyl azide substrate of at least a first protein in said cell, the synthetic isoprenyl azide substrate comprising at least a first azide;

b) contacting the cell with the synthetic isoprenyl azide substrate under conditions wherein the cell takes up and incorporates into the first protein at least athe first azide from the synthetic isoprenyl azide substrate to produce at least a first isoprenylated protein; and

c) detecting at least said first isoprenylated protein from proteins produced by said cell with a phosphine capture reagent by the Staudinger reaction.

2. (Currently amended) The method of claim 1, wherein the first protein is farnesylated.

3. (Original) The method of claim 1, wherein detecting comprises isolating the first protein.

4. (Original) The method of claim 2, wherein FPP is inhibited in said cell.

5. (Original) The method of claim 4, wherein FPP is inhibited by contacting the cell with an HMG Co-A reductase inhibitor.

6. (Original) The method of claim 4, wherein FPP is inhibited by contacting the cell with lovastatin.

7. (Previously presented) The method of claim 1, wherein the isoprenyl azide is further defined as an azido prenyl diphosphate.

8. (Withdrawn) The method of claim 1, wherein the isoprenyl azide is further defined as an azido isoprenyl alcohol.

9. (Original) The method of claim 1, wherein the isoprenyl azide is further defined as an azido farnesyl diphosphate.

10. (Withdrawn) The method of claim 1, wherein the isoprenyl azide is further defined as an azido farnesyl alcohol.

11. (Original) The method of claim 1, wherein the first protein is native to said cell.

12. (Original) The method of claim 1, wherein the step of detecting comprises Western blot analysis

13. (Original) The method of claim 1, wherein the phosphine capture reagent is bound to a solid support.

14. (Original) The method of claim 13, wherein the phosphine capture reagent is bound to a solid support with a photocleavable linker.

15. (Original) The method of claim 1, wherein the phosphine capture reagent comprises a label.

16. (Original) The method of claim 15, wherein the label comprises a fluorescent, colorimetric, chemiluminescent, or radioactive label.

17. (Original) The method of claim 15, wherein the label comprises an antigen.

18. (Original) The method of claim 17, wherein the antigen is biotin.

19. (Currently amended) The method of claim 18, wherein detecting <u>in step c)</u> comprises affinity-purification with streptavidin- and/or avidin-conjugated beads.

20. (Original) The method of claim 13, wherein the solid support comprises a bead composed of silica gel, polystyrene, starch, sugars, or organic or inorganic matrixes.

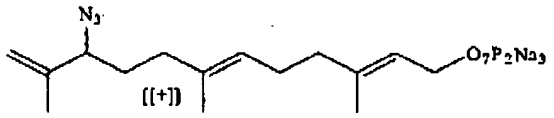
21. (Original) The method of claim 1, wherein a nucleophile in said Staudinger reaction is immobilized on a polymer.

22. (Original) The method of claim 21, wherein the polymer is selected from the group consisting of: mono-methyl polyethylene oxide, sepharose, tentagel, agrogel-Wang, polysaccharide, polystyrene, polyethane, and co-polymers thereof.

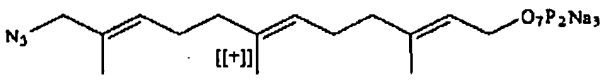
23. (Original) The method of claim 1, wherein the synthetic prenyl azide substrate is a substrate for a plurality of proteins and wherein the step of detecting comprises detecting the plurality of proteins.

24. (Currently amended) The method of claim 1, wherein the ~~prenylated~~ first protein is Ras.

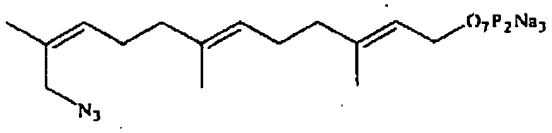
25. (Currently amended) The method of claim 1, wherein the synthetic isoprenyl azide substrate has the molecular formula:



26. (Currently amended) The method of claim 1, wherein the synthetic isoprenyl azide substrate has the molecular formula:



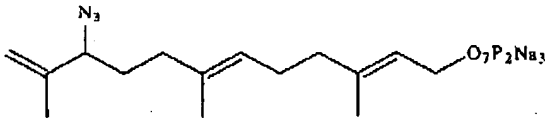
27. (Currently amended) The method of claim 1, wherein the synthetic isoprenyl azide substrate has the molecular formula:

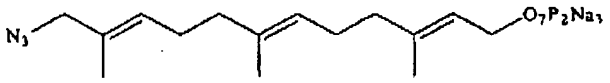


28. (Currently amended) A method for labeling a protein in a cell, comprising:

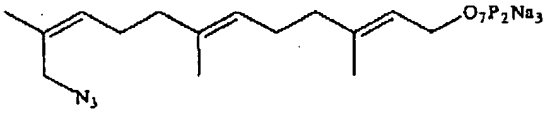
a) preparing a synthetic substrate of said protein by incorporating ~~comprising~~ at least a first azide in the synthetic substrate; and

b) contacting the cell with the synthetic substrate under conditions wherein the synthetic substrate is taken up and incorporated into the protein, ~~and~~ wherein the protein is labeled with said first azide and wherein the synthetic substrate has a molecular formula selected from the group consisting:



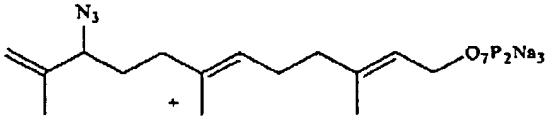


, and

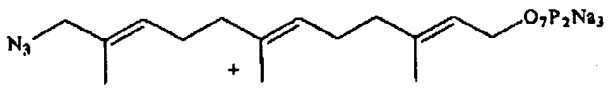


29. (Currently amended) The method of claim 28, wherein the synthetic substrate and the protein are~~is~~ prenylated.

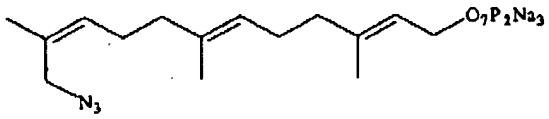
30. (Withdrawn) A compound having the molecular formula:



31. (Withdrawn) A compound having the molecular formula:



32. (Withdrawn) A compound having the molecular formula:



RESPONSE TO THIRD OFFICE ACTION

A. Status of the Claims

In response to the restriction requirement which the Examiner imposed, Applicants elected, without traverse, to prosecute claims 1-29, *i.e.*, the Group 1 claims and in response to an election of species requirement, Applicants elected the isoprenyl azide substrate comprising azido prenyl/farnesyl diphosphate. Claims 1-7, 9 and 11-29 are readable thereon and are presently under consideration. Claims 1, 2, 19 and 24-29 have been amended herein. Support for the amendments can be found in the claims as filed.

B. Specification Objections

(1) The specification is objected to for referring to "equation 1, herein above" at page 11, line 27. In response, Applicants note that reference to equation 1 has been deleted as unnecessary for an understanding of the invention. As indicated in the cited portion, equation 1 diagrammed the reduction that occurs during the known Staudinger reaction. As the reaction itself is well known and the working examples illustrate in detail its use in accordance with the invention, the equation is not necessary for describing the claimed invention. The objection is now moot and removal thereof is thus respectfully requested.

(2) The Action objects to page 18, scheme 1, and page 24, scheme 4, for the depiction of "+" adjacent to certain chemicals because it is not clear what chemical entity corresponds to "+." In response, Applicants note that the objection is moot in view of the specification amendment and removal of the objection is thus respectfully requested.

C. Rejection of Claims Under 35 U.S.C. §112, Second Paragraph

The Action rejects claims 1-7, 9 and 11-29 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out the subject matter which Applicant regards as the invention. The individual rejections and Applicants' responses are set forth below.

(1) The Action states that in step (a) of claim 1 the recitation of "isoprenyl azide substrate of at least a first protein" is grammatically awkward and is indefinite because it is not clear whether said "substrate" describes a substrate for said "azide" entity, or whether said "substrate" describes a substrate for said "protein" entity. Applicants respectfully traverse. The meaning of "isoprenyl azide substrate" is fully definite in view of the claims language. The full relevant term recites "a synthetic isoprenyl azide substrate **of at least a first protein** in said cell." (emphasis added). It is thus clear from the language of the claims that "substrate" modifies protein and refers to a substrate of the protein. The claim element is thus definite.

In addition, it is stated that it is not clear whether step (a) requires obtaining a first protein and/or a cell. In response, Applicants note that all required elements are recited by the claims and no basis to conclude otherwise has been presented. In step (a) one carrying out the invention need not obtain "a protein" as all that is recited and required is "obtaining a synthetic isoprenyl azide substrate of at least a first protein..." The "first protein" is an inherent element in the cell and the cell is already recited by the claim. The element of the cell is introduced in the preamble, and step (b) requires "contacting the cell under conditions wherein the cell takes up and incorporates into the protein at least a first azide from the substrate.." Thus step (b) entails the use of a cell and the element is already inherent in the claims. The claim as filed is thus fully definite in this respect as only those elements required to operate the claimed invention need be recited, which has fully been done here.

Finally, it is stated that the recitation of "a first protein" is indefinite because it is not clear whether "a first protein" corresponds to "a first isoprenylated protein" recited in the preamble. In response, it is noted that claim 1 has been amended and that the rejection is believed moot in view of the amendments.

In view of the foregoing, removal of the rejection is respectfully requested.

(2) The Action first states that in claim 1, step (b), the recitation of "a first azide" is indefinite because it is not clear whether "a first azide" corresponds to the "isoprenyl azide" of step (a), or whether "a first azide" describes a separate azide entity distinct from the "isoprenyl azide" of step (a). In response, Applicants note that claim 1 has been amended to clarify that the first azide comes from the isoprenyl azide. The rejection is believed moot in view of the amendments.

In addition, it is stated that the recitation of "incorporates into the protein at least a first azide from the substrate" is indefinite because it is not clear whether "a first azide" is incorporated into the protein, or whether both "a first azide" and "substrate" are incorporated into the protein. In response, it is noted that the claim has been amended to clarify that the first azide is incorporated into the protein. The claim neither requires or prevents the substrate itself from being incorporated into the protein as this is not required for the functioning of the claimed invention and, depending upon the substrate, the substrate itself may or may not be incorporated in the protein.

It is also stated that it is not clear whether "a first azide" and "substrate" are separate entities, or how "a first azide" and "substrate" become separate entities. In addition, the recitation of "contacting the cell" is said to be indefinite because it is not clear what entity is contacted with the cell. It is further stated that the recitation of "the protein" lacks antecedent

basis and is indefinite because it is not clear whether "the protein" corresponds to "a first protein" recited in step (a) or "a first isoprenylated protein" recited in the preamble. Finally, it is stated that the recitation of "the substrate" lacks antecedent basis and is indefinite because it is not clear whether "the substrate" corresponds to "a synthetic isoprenyl azide substrate" recited in step (a). In response, Applicants that claim 1 has been further clarified and that these rejections are believed moot in view of the amendments.

In view of the foregoing, removal of the rejection is respectfully requested.

(3) The Action states that in claim 1, step (c), the recitation of "proteins produced by said cell with a phosphine capture reagent" is indefinite because it is not clear how cells produce proteins "with a phosphine capture reagent." In response, Applicants note that "with a phosphine capture reagent" modifies" "detecting" and not "produced by said cell" and thus the meaning of the claim is not indefinite. This is the reading of the claims one of skill in the art would give while reading the full language of the claim in view of the teaching in the specification.

It is also stated that it is not clear whether the cell is contacted with "a phosphine capture reagent," or whether the cell produces "a phosphine capture reagent" endogenously. In response, Applicants note that the claim is fully definite as written. All that is required by the claim is that detecting at least said first isoprenylated protein from proteins produced by said cell be carried out "with a phosphine capture reagent by the Staudinger reaction." The source of the phosphine capture reagent is irrelevant to carrying out the invention. The claim element is thus fully definite.

In addition, it is stated that the recitation of "proteins produced by said cells ... by the Staudinger reaction" is indefinite because it is not clear how cell produce proteins by performing "the Staudinger reaction." In response, Applicants note as discussed above that "with a

phosphine capture agent by the Staudinger reaction" modifies "detecting" and not "produced by said cell..." It is thus believed that the rejection is moot.

It is also stated that the recitation of "detecting at least said first protein ... with a phosphine capture reagent" is indefinite because it is not clear whether said first protein is contacted with a phosphine moiety, or whether said first protein is produced with a phosphine moiety by said cell. In response, Applicants note as also described above that phosphine capture reagent modifies "detecting." It is thus clear that the phosphine capture agent is used during detecting but is not required in order to obtain "proteins produced by said cell." It is thus believed that the rejection is now moot.

Finally, it is stated that the recitation of "said first protein" is indefinite because it is not clear whether "said first protein" corresponds to "the protein" recited in step (b) or "a first isoprenylated protein" recited in the preamble. In response, it is noted that the rejection is now believed moot in view of the amendments to claim 1.

In view of the foregoing, removal of the rejection is respectfully requested.

(4) Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps. Specifically, it is stated that the preamble of claim 1 does not appear to correspond to the method outcome. It is also stated that it is not clear how merely detecting "said first protein" amounts to detecting "a first isoprenylated protein." It is further stated that it is not clear whether "said first protein" corresponds to "the protein" recited in step (b) or "a first isoprenylated protein" recited in the preamble. Finally, it is stated that it is not clear whether additional method steps are required to detect "a first isoprenylated protein." In response, Applicants note that all of the concerns of the Examiner are believed to be rendered moot in view of the amendments to claim 1.

In view of the foregoing, removal of the rejection is respectfully requested.

(5) The Action states that, in claim 2, the recitation of "the protein is farnesylated" is indefinite because it is not clear during which step(s) of claim 1 said protein is farnesylated.

In response, Applicants note that claim 2 has been amended to recite that "the protein" refers to "the first protein" from claim 1. The claim is therefore fully definite and the rejection is now moot.

In view of the foregoing, removal of the rejection is respectfully requested.

(6) The Action states that, in claims 4-6, the recitation of "FPP" lacks antecedent basis. In response, Applicants note that FPP is naturally produced by cells and thus is inherently present in a cell. FPP therefore has an antecedent basis in "cell" and the use of the term is not indefinite.

In addition, it is stated that the recitation of "FPP is inhibited" is indefinite because the physical parameters underlying the process of inhibition, as well as the standard or degree of inhibition required by "inhibited" is not clear. In response, Applicants note that breadth is not indefiniteness. All that the claim requires and is relevant is that FPP be inhibited. The benefits of such inhibition and are explained in the specification. The mechanism by which this occurs is irrelevant. "Inhibited" further has a well known meaning in the art. The term as used is thus fully definite.

It is finally stated that it is not clear how "HMG Co-A reductase inhibitor" and "lovastatin" inhibit FPP. In response, Applicants note that the specification explains at page 13 that "Lovastatin, a HMG CoA reductase inhibitor, blocks mevalonate synthesis, and therefore leads to inhibition of FPP synthesis and protein farnesylation (Sinensky, 1990; Kim, 1990)." It is

further noted that the claim need not recite this information as it is known in the art and not required for the function and use of the claimed method. The claim is thus definite.

In view of the foregoing, removal of the rejection is respectfully requested.

(7) The Action states that, in claim 12, it is not clear how "Western blot analysis" is incorporated into the method of claim 1. In response, Applicants note that claim 12 specifics that "the step of detecting comprises Western blot analysis" and that the detecting step is set forth in step (c) of claim 12. For example, step (c) requires "detecting at least said first isoprenylated protein from proteins produced by said cell with a phosphine capture reagent by the Staudinger reaction." Claim 12 therefore specifies where in claim 1 Western blot analysis is incorporated and claim 1 specifies all of the required elements of the claim. It is further noted that use of Western blot analysis in the context of the claimed invention is illustrated in the working examples. The claim language as thus clear on its face and even more so when considered in view of the specification.

It is also stated that it is not clear whether "Western blot analysis" is performed in addition to step (c). In response, Applicants note that claim 12 requires that "the step of detecting comprises Western blot analysis..." It is thus clear from the claim language that claim 12 defines step (c) and does not require an additional step, although one of skill in the art would of course not be precluded from carrying out such an additional step should they choose to do so.

In view of the foregoing, removal of the rejection is respectfully requested.

(8) The Action states that, in claim 19, it is not clear how "affinity-purification" is incorporated into the method of claim 1. It is also stated that it is not clear whether "affinity-purification" is performed in addition to step (c). In response, Applicants note that the claim has been amended herein. It is believed that the rejection is now moot.

In view of the foregoing, removal of the rejection is respectfully requested.

(9) The Action states that, in claim 20, the recitation of "a bead" is indefinite because it is not clear whether a single bead is intended. In response, Applicants note that the claim only requires one bead, as this is all that is required for the function of the claimed invention. Specifically, while one of skill in the art may choose to use a plurality of beads, only one bead is required to carry out the claims. The claims are thus fully definite.

In view of the foregoing, removal of the rejection is respectfully requested.

(10) In claim 21, it is not clear how "a nucleophile" is incorporated into the method of claim 1 or whether "a nucleophile" correlates to any entity recited in claim 1. In response, Applicants note that the claim depends from claim 1 and further specifies that "a nucleophile in said Staudinger reaction is immobilized on a polymer." The claim therefore further defines how the Staudinger reaction is carried out in claim 1. The Staudinger reaction is only required in step c) of claim 1 and thus the claim refers to and further defines step c). It is therefore clear where in "a nucleophile" is incorporated into the method of claim 1 and further which entity it refers to.

In view of the foregoing, removal of the rejection is respectfully requested.

(11) The Action states that, in claim 24, the recitation of "the prenylated protein" lacks antecedent basis. In response, Applicants note that the claim has been amended to correct the antecedent basis and that the rejection is now believed to be moot.

In view of the foregoing, removal of the rejection is respectfully requested.

(12) The Action states that, in claims 25-26, the incorporation of "+"adjacent to the recited molecular formulas is indefinite because it is not clear what chemical entity corresponds or correlates to. In response, Applicants note that the claims have been amended and that it is believed that the rejection is moot in view of the amendments.

In view of the foregoing, removal of the rejection is respectfully requested.

(13) The Action states that, in claim 28, step (a) is grammatically awkward and is indefinite because it is not clear whether "a synthetic substrate" comprises "a first azide", or whether "said protein" comprises "a first azide." In response, Applicants note that the claim has been amended and that it is believed that the rejection is moot in view of the amendments.

In view of the foregoing, removal of the rejection is respectfully requested.

(14) The Action states that, in claim 29, the recitation of "synthetic" is indefinite because it is not clear how a prenylated substrate is "synthetic." In addition, it stated that it is not clear how a prenylated substrate is incorporated into the method of claim 28. It is not clear how a prenylated substrate is "incorporated into the protein." In response, Applicants note that the claim has been amended and that it is believed that the rejection is moot in view of eh amendments.

In view of the foregoing, removal of the rejection is respectfully requested.

D. Rejections Under 35 U.S.C. §102

The Action rejects claims 28-29 as being anticipated by Spielmann et al. (US 6,284,910). In particular, it is stated that Spielmann et al. teach a method for labeling a protein (citing col. 27, lines 14-15, "H-Ras farnesyl-group") in a cell (citing col. 27, line 12, "oocytes") comprising the steps of: obtaining a synthetic substrate of said protein (citing col. 27, line 17, "farnesyl analogs") comprising an azide (citing col. 6, line 52, "N_3"), and contacting the cell under conditions wherein the synthetic substrate is taken up (citing col. 27, line 18, 'microinjection") and incorporates (citing col. 27, lines 16-17, "enzymatic methods to attach") into the protein (citing col. 27, line 17, "H-Ras") and wherein the protein is labeled with said first azide (citing col. 27, lines 14-15, "H-Ras farnesyl-group").

In response, Applicants respectfully traverse but notc that claim 28 has been amended herein and that the rejection is now moot. Removal of the rejection is thus respectfully requested.

E. Rejections Under 35 U.S.C. §103(a)

1. Rejection of claims 1-7, 9, 11, 13 and 15-24

The Action rejects claims 1-7, 9, 11, 13 and 15-24 under 35 U.S.C. §103 as being obvious over Spielmann et al. (US 6,284,910) in view of Saxon and Bertozzi (US 6,570,040). In particular, it is asserted that Spielmann et at. teach detecting an isoprenylated protein (citing col. 27, lines 14-1 5, "H-Ras farnesyl-group") in a cell (citing col. 27, line 12, "oocytes') by: obtaining a synthetic isoprenyl (citing col. 27, line 17, "farnesyl analogs") azide (citing col. 6, line 52, "N;) substrate of a protein (citing col. 26, line 3, "FTase"), contacting the cell under conditions wherein the cell takes up (see col. 27, line 18, "microinjection") and incorporates (citing col. 27, lines 16-17, "enzymatic methods to attach") into the protein (citing col. 27, line 17, "H-Ras") a first azide (citing col. 6, line 52, "N3") from the substrate (citing col. 27, line 17, "farnesyl analogs"), and detecting (citing col. 25, line 66, "Assay for Analog Transfer") said protein (citing col. 26, line 3, "FTase"). It is stated that Spielmann et al. do not teach "a phosphine capture reagent" or "the Staudinger reaction" but that Saxon & Bertozzi teach this element for detecting intracellular azido-target substrates (citing col. 14, line 57, "detectable labels", line 55, "intracellular", lines 52-53, "azido-target substrate"). Therefore, it is concluded that it would be obvious to detect an isoprenylated protein according to Spielmann et al. with a phosphine capture reagent and the Staudinger reaction because Saxon & Bertozzi discovered that the Staudinger reaction is both selective and compatible with aqueous environments, thereby allowing *in vivo* applications (citing Abstract).

Applicants respectfully traverse. The claims are not obvious as one of skill in the art would have lacked a motivation to combine the cited references to arrive at the claimed invention absent impermissible hindsight reconstruction based on the teaching in the specification. The Spielmann et al. reference deals with a different problem than that solved by the claimed invention. Specifically, Spielmann concerns a specific FPP analog and therapeutic implications of this rather than detecting an isoprenylated protein in a cell as claimed. The analogs modify functional groups and thus the biological activity of prenyl-protein specific enzymes. *See, e.g.*, col. 28, l. 7-11. The Spielmann reference further deals in this regard narrowly with the "design and synthesis of a farnesylpyrophosphate (FPP) analog, 8-anilinogeranyl pyrophosphate (AGPP) that is transferred to Ras by farnesyltransferase (FTase), in which the omega-terminal isoprene unit of the farnesyl group has been replaced with an aniline functionality." It is further stated that:

> The compounds of this invention inhibit farnesyl-protein transferase and the farnesylation of the oncogene protein Ras. These compounds are useful as pharmaceutical agents for mammals, especially for humans. These compounds may be administered to patients for use in the treatment of cancer.

Col. 11, l. 28-32. The application goes on to describe in great detail the formulation of pharmaceutical compositions for delivering such therapeutic agents. The patent thus relates to therapeutic rather than diagnostic applications and one of skill in the art would be without any motivation to combine this reference with Saxon & Bertozzi absent hindsight reconstruction.

While a section in cols. 28-29 of Spielmann is cited that mentions a "continuous fluorescence assay for analog transfer" a further review demonstrates that this *in vitro* assay is of the ability to transfer FPP analogs to substrates by FTase, rather than detection of isoprenylated proteins, let alone detection of proteins from a cell. For example, the section states that "An important requirement for these studies is the development of a rapid technique for evaluating

whether FPP analogs that are efficiently and appropriately transferred to target substrates by FTase. The analogs were evaluated for their ability to be transferred by FTase to the pentapeptide N-dansyl-GCVLS in a continuous fluorescence assay." The section therefore goes to confirming the ability to produce analogs, not detection of proteins. This therefore has no relevance to the claimed invention.

The Action also cites col. 27 as teaching *in vivo* application of the technique, yet this section deals with a different technique. The section indicates that what is microinjected is modified H-Ras, rather than a substrate of H-Ras. For example, it is stated that "The approach makes use of enzymatic methods to attach structurally related farnesyl analogs onto the prenylation site of H-Ras combined with microinjection procedures to study their in vivo function." Col. 27, l. 15-19. The technique is used to examine the biological activity of the analog, not detect an isoprenylated protein in a cell, this section stating that "the system provides a method to study the in vivo role of prenylation by analyzing the ability of FPP analogues to rescue H-Ras biological functions in isoprenoid-depleted oocytes."

In sum, one of skill in the art would have been without any motivation to combine the cited references based on the prior art and absent application of impermissible hindsight reconstruction. *See In re Carroll*, 202 USPQ 571 (CCPA 1979) ("One of the more difficult aspects of resolving questions of non-obviousness is the necessity 'to guard against slipping into the use of hindsight.'"), citing *Graham v. John Deere Co.*, 148 USPQ 459 (U.S. Sup. Ct. 1965). In order to establish a *prima facie* case of obviousness under 35 U.S.C. §103 "substantial evidence" demonstrating the motivation to combine the references must be shown on the record. *See In re Vaeck*, 947 F.2d 488, 20 USPQ 2d 1438 (Fed. Cir. 1991), *see also In re Zurko*, 59

USPQ 2d 1693 (Fed. Cir. 2001). As such evidence is lacking, removal of the rejection is respectfully requested.

2. Rejection of claim 12

Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Spielmann et al. (US 6,284,910) and Saxon & Bertoui (US 6,570,040) as applied to claim 1, and further in view of Lodish et al., MOLECULAR CELL BIOLOGY, 4th ed., W.H. Freeman & Co. (1999). In particular, it is stated that Spielmann et al. and Saxon & Bertoui teach detecting an isoprenylated protein as described supra but do not teach Western blot detection. It is stated that Lodish et al. teach this element for detecting a particular protein in a mixture (see Section 3.5) and thus it would be obvious to detect an isoprenylated protein with Western blot detection because Lodish et al. teach Western analysis is "one of the most powerful methods for detecting a particular protein" combining "superior resolving power of gel electrophoresis, the specificity of antibodies, and the sensitivity of enzyme assays."

In response, Applicants note that claim 12 depends from claim 1 and incorporates all limitations of the claim. As the rejection does nothing to cure the shortcomings with respect to claim 1, claim 12 is by definition also nonobvious for the reasons set forth above. Removal of the rejection is thus respectfully requested.

3. Rejection of claim 14

The Action rejects claim 14 under 35 U.S.C. 103(a) as obvious over Spielmann et al. (US 6,284,910) and Saxon & Bertozzi (US 6,570,040) as applied to claims 1 and 13, and further in view of Holmes, 62 J. ORG. CHEM. 2370 (1 997). Spielmann et at. and Saxon & Bertozzi are said to teach detecting an isoprenylated protein and Saxon & Bertozzi additionally a cleavable linker. It is stated that these do not teach a photocleavable linker but that Holmes teaches

photocleavable linkers for anchoring biomolecules to solid supports. Therefore, it is concluded that it would be obvious to replace the cleavable linker of Saxon & Bertozzi with a photocleavable linker because Holmes states that photocleavable linkers are "particularly attractive in combinatorial library screening," as they result in biomolecules that are free of cleavage reagents.

In response, Applicants note that claim 14 depends from claim 1 and incorporates all limitations of the claim. As the rejection does nothing to cure the shortcomings with respect to claim 1, claim 14 is by definition also nonobvious for the reasons set forth above. Removal of the rejection is thus respectfully requested.

In view of the foregoing, Appellants respectfully request the removal of the rejection under 35 U.S.C. § 103.